The Evolving Spectrum of the Epidemiology of Thalassemia

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KEYWORDS

• Thalassemia • Global frequency • Malaria • Future frequency
• North/South partnerships • Future control

KEY POINTS

- The current frequency and global load of the thalassemias are discussed.
- An estimation of the frequency for the foreseeable future is discussed.
- The reasons for the high frequency of thalassemia are discussed.
- The development of partnerships between the poor and richer countries for the better control and management of thalassemia is discussed.

INTRODUCTION

The inherited disorders of hemoglobin (Hb), which include sickle cell anemia and its variants and the thalassemias, are the most common monogenic diseases.[1,2] There are 2 main forms of thalassemia, α and β thalassemia. The α globin genes, which are duplicated, are on chromosome 16. A deletion of one of them is termed α^+ thalassemia, whereas if both of the pair are deleted it is termed α^0 thalassemia. Point mutations of the α genes are much less common; only one, Hb Constant Spring, occurs at a very high frequency in some populations. The single β globin genes are on chromosome 11. The β thalassemias result from more than 200 different mutations, and deletions are much less common. There is a very common structural Hb variant, Hb E, which is synthesized at a reduced rate and behaves like a very mild form of β thalassemia. When inherited together with β thalassemia, the result is Hb E β thalassemia, which is one of the most common forms of severe thalassemia in many parts of Asia.

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The α^+ thalassemias alone are not associated with any severe hematologic changes; their major importance is that when they are inherited together with different forms of β thalassemia, they tend to reduce the severity of the disease. Coinheritance of α^+ and α^0 thalassemia results in a condition of variable severity called Hb H disease, whereas homozygosity for α^0 thalassemia results in hydrops fetalis and death in utero or early after birth. The β thalassemias are divided into β thalassemia major or intermedia depending on the severity of the particular mutations or the inheritance of phenotypic modifiers. Hb E β thalassemia is associated with remarkable variability of the phenotype, ranging from severe β thalassemia major through various levels of β thalassemia intermedia.

Although much progress has been made toward the prevention and management of the thalassemias in the richer countries, this is not the case for many of the poorer countries of the tropical belt. In this article, current knowledge about the world distribution and frequency is discussed together with the reasons for the very high frequency of the different forms of thalassemia. Particular emphasis is placed on likely changes in the frequency of thalassemia in the future and the effects of changes in the environment and of population movement on the global health load caused by this disease. The danger of its continued neglect by international health agencies is also discussed.

WORLD DISTRIBUTION

An approximate distribution of the α and β thalassemias is shown in **Figs. 1** and **2**, respectively, and summarized in references.[1,2] The α^+ thalassemias, which spread at high frequency right across the tropical belt from sub-Saharan Africa through the Middle East, South Asia, and Southeast Asia, are undoubtedly the most common of all single

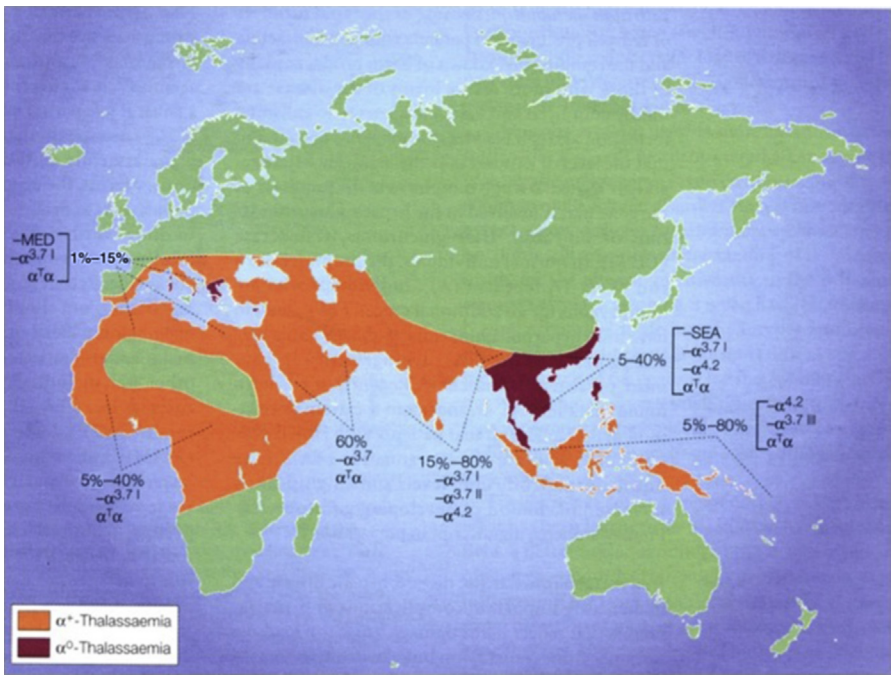

Fig. 1. The approximate distribution of the α thalassemias. (*From* Weatherall DJ. Phenotype-genotype relationships in monogenic disease: lessons from the thalassaemias. Nat Rev Genet 2001;2(4):245–55; with permission.)